Oncology Clinical Pathways
Lung Cancer
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# Table of Contents

- NSCLC Clinical Stage IA and IB ................................................................. 3
- NSCLC Clinical Stage IIA, IIB, and Resectable IIIA Excluding Pancoast Tumors for Patients Who Have Not Received Neoadjuvant Treatment .......... 4
- NSCLC Clinically Resectable Stage IIA, IIA, and IIIA Excluding Pancoast Tumors ................................................................. 5
- Pancoast Tumors T4N1 or T4N0 ................................................................. 6
- NSCLC Stage III Unresectable Multiple Level N2, Bulky N2, Any N3, Any T4 due to Tumor Invasion into Adjacent Structure First Line ................. 7
- Molecular Testing .................................................................................. 8
- NSCLC Stage IVA M1b Single Extrathoracic Site (Oligometastatic Disease) or M1a due to a Contralateral Nodule at Presentation .......... 9
- NSCLC Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Positive ................................................................. 10
- NSCLC Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative ................................................................. 11
- Non-Squamous Relapse ....................................................................... 12
- Squamous Stage IVB First Line ............................................................. 13
- Squamous Relapse ............................................................................... 14
- SCLC Incidental Discovery .................................................................. 15
- SCLC Limited Stage First Line ............................................................. 16
- SCLC Extensive Stage First Line ........................................................... 17
- SCLC Relapse ...................................................................................... 18
Lung Cancer – NSCLC Clinical Stage IA and IB

After multidisciplinary discussion, patient a surgical candidate?

Yes

Lobectomy resection with lymph node sampling

Pathological stage consistent with clinical stage?

Yes

Margin status?

Yes

Re-resection candidate?

Yes

Re-sect

Negative

Surveillance

No

Follow appropriate pathway based on pathological stage

No

Refer to Radiation Oncology

NSCLC Clinical Stage IA and IB

Clinical trial(s) always considered on pathway.

*a If contraindications to lobectomy, sublobar resection may be considered; segmentectomy is preferred

*b Lymph node sampling is strongly encouraged as part of standard of care during surgical resection; minimum recommendation should include examination and/or sampling of >3 mediastinal and ≥1 hilar station
Lung Cancer – NSCLC Clinical Stage IIA, IIB, and Resectable IIIA Excluding Pancoast Tumors for Patients Who Have Not Received Neoadjuvant Treatment

Clinical trial(s) always considered on pathway.

* Lung-sparing anatomic resection (sleeve lobectomy) preferred over pneumonectomy if anatomically appropriate and margin-negative resection can be achieved

° Lymph node sampling is strongly encouraged as part of standard of care during surgical resection; minimum recommendation should include examination and/or sampling of >3 mediastinal and >1 hilar station

° PD-L1 expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

CGP Comprehensive Genomic Profiling
Lung Cancer – NSCLC Clinically Resectable Stage IIA, IIB, and IIIA Excluding Pancoast Tumors

NSCLC Clinically Resectable Stage IIA, IIB, and IIIA Excluding Pancoast Tumors

Multidisciplinary discussion

Candidate for surgery and neoadjuvant chemimmune therapy?

Yes

Perform PD-L1 by TPS and CGP a b c

Yes

Follow NSCLC Stage III Unresectable Multiple Level N2, Bulky N2, Any N3, Any T4 Line pathway

Non-squamous: pemetrexed or paclitaxel, cisplatin d and nivolumab (every 3 weeks for 3 cycles)

Squamous: gemcitabine or paclitaxel, cisplatin d and nivolumab (every 3 weeks for 3 cycles)

EGFR mutation or ALK translocation positive?

Yes

Surgery

Follow NSCLC Clinical Stage IIA, IIB, and Resectable IIIA Excluding Pancoast Tumors for Patients Who Have Not Received Neoadjuvant Treatment

No

Surgery

Margin status?

R0

Surveillance

R1 or R2

Re-resection candidate?

Yes

Re-resect

No

Refer to Radiation Oncology

a PD-L1 expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

b PD-L1 subgroup analysis did not show statistical improvement in event free survival for patients PD-L1 <1%; greatest benefit for neoadjuvant chemotherapy with immunotherapy was noted in Stage III patients

c CGP is indicated because patients with known EGFR mutations or ALK translocations were excluded from CheckMate 816 study establishing the role of neoadjuvant chemotherapy with immunotherapy

d If contraindication to cisplatin prescribe carboplatin

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Clinical trial(s) always considered on pathway.
Lung Cancer – Pancoast Tumors T4N1 or T4N0

After multidisciplinary discussion, patient a surgical candidate?

- Yes
  - Contraindication to cisplatin and etoposide? *
    - Yes
      - Cisplatin and etoposide (2-3 cycles) with concurrent radiation
    - No
      - Surgery

- No
  - Contraindication to cisplatin and etoposide? *
    - Yes
      - Carboplatin and paclitaxel (2-3 cycles) with concurrent radiation
    - No
      - Carboplatin and etoposide (2-3 cycles) with concurrent radiation

Clinical trial(s) always considered on pathway.

* Contraindications include abnormal renal function, ECOG 2, or abnormal heart function
Lung Cancer – NSCLC Clinical Stage III Unresectable Multiple Level N2, Bulky N2, Any N3, Any T4 Due To Tumor Invasion Into Adjacent Structure First Line

NSCLC Stage III Unresectable Multiple Level N2, Bulky N2, Any N3, Any T4 due to Tumor Invasion into Adjacent Structure First Line

Perform PD-L1 by TPS and CGP*

After multidisciplinary discussion, qualify for definitive radiation?

Yes

Candidate for concurrent?

Yes

Carboplatin and paclitaxel 6 weeks with concurrent chest radiation

Progression?

Yes

Follow Stage IV Pathway

No

Contraindication to immunotherapy?

Yes

Follow Stage IV pathway

No

Surveillance

Non-squamous: carboplatin and pemetrexed (3 cycles) followed by definitive radiation

Progression?

Yes

Follow Stage IV Pathway

No

Surveillance

Squamous: carboplatin and paclitaxel (3 cycles) followed by definitive radiation

Yes

Follow Stage IV Pathway

No

Surveillance

Clinical trial(s) always considered on pathway.

*PD-L1 expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information; CGP is indicated because the role of consolidation durvalumab is unclear in EGFR mutant or ALK translocation positive patients

CGP Comprehensive Genomic Profiling
Lung Cancer – Molecular Testing

Molecular Testing

- Order CGP on tumor tissue (non-squamous)
- Order PD-L1 by TPS testing

Is tissue biopsy sufficient?

- Yes
- No

Repeat biopsy possible?

- Yes
- No

Repeat biopsy

Perform liquid biopsy if concern for progressive disease
Lung Cancer – NSCLC Stage IVA M1b Single Extrathoracic Site or M1a Due To A Contralateral Nodule at Presentation

Clinical trial(s) always considered on pathway.

*a PD-L1 expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information

CGP Comprehensive Genomic Profiling
Lung Cancer – NSCLC Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Positive

**NSCLC-Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Positive**

- Refer to Palliative Care
- Perform PD-L1 by TPS and CGP
- Targeted treatment based on genomic analysis

Clinical trial(s) always considered on pathway.

- **Pericardial/Pleural Effusion** Appropriate local therapy for malignant effusion should be pursued
- If patient has limited brain metastases M1c, consider referral to Radiation Oncology for SRS
- PD-L1 expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information
- Targetable Treatment If targetable mutation not standard, submit NPOP consult
- Genomic Analysis If delayed genomic results and patient is symptomatic, hold immunotherapy for first cycle and proceed with chemotherapy

**CGP Comprehensive Genomic Profiling**

First Line

- EGFR Exon 19 Deletion or Exon 21 L858R Mutation
  - Biopsy confirmed transformation to SCLC?
  - Yes
  - Follow SCLC pathway
  - No
  - Carboplatin and pemetrexed +/- checkpoint inhibitor
  - Doxorubicin

- ALK Gene Fusion
  - Alectinib
  - Lorlatinib

- KRAS G12C
  - Refer to NSCLC-Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative pathway

- EGFR Exon 20 Insertion
  - Refer to NSCLC-Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative pathway

- HER2 Mutation
  - Refer to NSCLC-Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative pathway

Second Line

- MET Exon 14 Skipping Mutation
  - Capmatinib

- RET Rearrangement
  - Selpercatinib

- ROS1 Gene Fusion
  - Entrectinib

- BRAF V600E
  - Dabrafenib and trametinib

- NTRK Gene Fusion
  - Entrectinib

Subsequent Treatment

- Carboplatin and pemetrexed +/- checkpoint inhibitor
- Doxorubicin

Biopsy confirmed transformation to SCLC? No Yes

Clinical trial(s) always considered on pathway.
Lung Cancer – NSCLC Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative

NSCLC-Stage IVA Due to Pericardial/Pleural Effusion and IVB Mutation Negative

Refer to Palliative Care

Candidate for chemotherapy?

Yes

PD-L1 ≥1%?

Yes

Pembrolizumab

No

Hospice

No

PD-L1 expression 0-49% or unknown

Yes

Immunotherapy contraindication

PD-L1 expression ≥50%

Pembrolizumab with carboplatin with pemetrexed; pemetrexed-pembrolizumab maintenance (up to 2 years)

OR

Pembrolizumab with carboplatin with pemetrexed; pembrolizumab alone

Immunotherapy contraindication

Carboplatin with pemetrexed (4 cycles) followed by maintenance pemetrexed

Clinical trial(s) always considered on pathway.

* Pericardial/Pleural Effusion appropriate local therapy for malignant effusion should be pursued

No

Refer to Palliative Care
Lung Cancer – Non-Squamous Relapse

Non-Squamous 2nd Line Progression Chemotherapy with or without Immunotherapy

- **KRAS G12C, EGFR Exon 20 Insertion, or HER2 mutation found?**
  - Yes: Sotorasib (KRAS G12C)
  - Yes: EGFR Exon 20 Insertion
  - Yes: Trastuzumab deruxtecan (HER2/ERBB2 mutation and/or amplification) *
  - No: Docetaxel

**Patient preference after shared decision making**

- Yes: Mobocertinib b
- Yes: Amivantamab c

Non-Squamous 2nd Line Progression Immunotherapy Alone

- Carboplatin and pemetrexed (4 cycles)

**Progression?**

- Yes: Docetaxel
- No: Continue maintenance pemetrexed

**Non-Squamous 3rd Line Progression**

- Patient received docetaxel? (if limited progression, consider referral to Radiation Oncology)
  - No: Docetaxel
  - Yes: Clinical trial or refer to Hospice

Clinical trial(s) always considered on pathway.

*HER2/ERBB2 positive mutation and/or amplification consider consult to the National Precision Oncology Program (NPOP) regarding treatment

b **Mobocertinib** do not use if you can’t avoid use of other drugs that prolong the QTc interval, or with moderate or strong CYP3A4 inhibitors (Boxed Warning)

c **Amivantamab** do not use if patient has transportation issues, cannot take pre-medications, or prefers to avoid prolonged exposure in facility

d **Progression** if limited progression, consider referral to Radiation Oncology
**Lung Cancer – Squamous Stage IVB First Line**

- **Refer to Palliative Care**
- **Multidisciplinary discussion a**
- **Never/light smoker, mixed histology, small specimen size, or clinically indicated?**
  - **No**
  - **Qualify for chemotherapy?**
    - **No**
    - **Perform PD-L1 by TPS and CGP b**
    - **Yes**
      - **PD-L1 expression 0-49% or unknown**
      - **PD-L1 expression ≥ 50%**
        - **Immunotherapy contraindication**
        - **Pembrolizumab, carboplatin and paclitaxel (4 cycles) followed by pembrolizumab alone maintenance for up to 2 years c**
  - **Yes**
    - **Qualify for immunotherapy?**
      - **No**
        - **Pembrolizumab**
      - **Yes**
        - **PD-L1 ≥1%?**
          - **Yes**
            - **Pembrolizumab**
          - **No**
            - **Hospice**

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* a If patient is symptomatic refer to Radiation Oncology
  
* b PD-L1 expression should be performed using 22C3 antibody and determined by TPS score; follow Molecular Testing pathway for further information
  
* c If limited progression, consider referral to Radiation Oncology and continuation of first-line systemic therapy
  
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Lung Cancer – Squamous Relapse

**Squamous 2nd Line Progression on Chemotherapy +/- Immunotherapy**

- Progression in ≤4 sites that are amenable to radiation?
  - Yes: Refer to Radiation Oncology for local therapy
  - No: Docetaxel

**Squamous 2nd Line Progression on Immunotherapy Alone**

- Progression in ≤4 sites that are amenable to radiation?
  - Yes: Refer to Radiation Oncology for local therapy
  - No: Carboplatin and paclitaxel (4-6 cycles)

**Squamous 3rd Line Progression**

- Progression in ≤4 sites that are amenable to radiation?
  - Yes: Refer to Radiation Oncology for local therapy
  - No: Clinical trial or refer to Palliative Care

Clinical trial(s) always considered on pathway.
Lung Cancer – SCLC Incidental Discovery Resected T1, T2 N0 M0

Completely resected T1-2 N0 M0 pathologic stage?

- Yes
  - Cisplatin and etoposide (4 cycles) without chest radiation

- No
  - Cisplatin and etoposide (4 cycles) with chest radiation

Clinical trial(s) always considered on pathway.
**Lung Cancer – SCLC Limited Stage First Line**

1. SCLC Limited Stage First Line
2. Multidisciplinary discussion
3. Contraindication to cisplatin and etoposide?
   - Yes: Carboplatin and etoposide (4 cycles) concurrently with chest radiation
   - No: Cisplatin and etoposide (4 cycles) concurrently with chest radiation
4. Order CT scan (abdomen/chest/pelvis) and MRI with and without contrast (brain)
5. Progression?
   - Yes
     - Brain MRI and systemic surveillance as clinically indicated
   - No: Follow SCLC Relapse pathway

Clinical trial(s) always considered on pathway.

*In the rare case of T1-2 N0 M0, surgery can be considered followed by adjuvant chemotherapy*

*Contraindications include abnormal renal function, ECOG 2, or abnormal heart function*

*Initiate radiation as early as possible, within the first or second cycle of chemotherapy*
Lung Cancer – SCLC Extensive Stage First Line

**Contraindication to chemo/immuno therapy?**
- Yes → Symptomatic metastases or unlikely to respond to systemic therapy?
  - Yes → Refer to Hospice
  - No → Immunotherapy contraindication
- No → Carboplatin with etoposide (4-6 cycles) with atezolizumab

**Progression?**
- Yes → Follow SCLC Relapse pathway
- No → Chemotherapy contraindication

**Maintenance atezolizumab until progression or toxicity**

If less than complete response, refer to Radiation Oncology for chest radiotherapy

Clinical trial(s) always considered on pathway.

Refer to Palliative Care

Refer to Radiation Oncology
Lung Cancer – SCLC Relapse

SCLC Relapse

- Refer to Palliative Care
- Refer to Radiation Oncology if symptomatic metastases

Time to progression?

- < 6 months:
  - PS 0-1:2: Lurbinectedin
  - PS 3-4: Refer to Hospice

- > 6 months:
  - Carboplatin and etoposide (4-6 cycles)
  - Progression?
    - Restart pathway

Clinical trial(s) always considered on pathway.

- If patient is progressing and did not receive immunotherapy upfront, patient can receive carboplatin, etoposide, and atezolizumab
Questions?

Contact VHAOncologyPathways@va.gov